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### INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(51) International Patent Classification 5:		(11) International Publication Number: WO 94/07
A61K 31/05, 9/00, 47/02 A61K 47/14	A1 ·	(43) International Publication Date: 14 April 1994 (14.0
(21) International Application Number: PCT/US (22) International Filing Date: 5 October 1993		pean patent (AT, BE, CH, DE, DK, ES, FR, GB,
(30) Priority data: 07/958,069 7 October 1992 (07.10.92	2)	Published US With international search report.
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(54) Title: TASTE MASKING OF THYMOL		

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#### (57) Abstract

An aqueous composition or final product containing thymol comprises sodium chloride and menthol lactate for masking the unpleasantly medicinal flavor of thymol, an essential oil with antimicrobial properties. In particular, the invention describes an embodiment wherein the ratio of sodium chloride to thymol is about 7.8 to 1 and the ratio of menthyl lactate to thymol is about 0.3 to 1.

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# TASTE MASKING OF THYMOL THE FIELD OF THE INVENTION

This invention is directed to compositions containing thymol in which the unpleasant, medicinal, or harsh taste of thymol is masked by the presence of sodium chloride and menthyl lactate.

## BACKGROUND OF THE INVENTION

Thymol is an essential oil which is well known for its antimicrobial ability in several kinds of In particular, thymol can be useful in 10 preparations. oral hygiene products such as mouth rinses, when present in sufficient quantities to insure the desired beneficial therapeutic effects. However, thymol imparts a penetrating flavor to the product which is perceived as unpleasant, medicinal or even harsh by the user of the 15 product. It would therefore be desirable to endeavor preparing thymol containing products which possess a pleasant acceptable taste. In addition, this taste masking preparation of thymol would be attained in the absence of overwhelming amounts of flavoring agents which 20 would create a disharmonious overall flavor perception not desirable in the final product.

U.S. Patent No. 4,985,087 to Talivar, et al. discloses a composition containing thymol in which the harsh taste of thymol has been masked utilizing substantial amounts of a sugar alcohol or a mixture of sugar alcohols, and anethole, wherein the ratio of the sugar alcohol to the thymol ranges from about 1750:1 to about 200:1 and the ratio of the anethole to thymol ranges from about 0.1 to about 1.75:1.

#### SUMMARY OF THE INVENTION

Therefore, the present invention provides a welcome composition of final product containing thymol in which the harsh, medicinal taste of thymol has been effectively masked by the presence of relatively low levels of sodium chloride and menthyl lactate. Sodium chloride and menthyl lactate are present in amounts below

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which levels the unpleasant taste perception of the thymol is not effectively masked. The presence of sodium chloride and menthyl lactate in sufficient amounts masks the unpleasant taste of thymol providing the user of the product or consumer with acceptably pleasant taste perception.

Further, the present invention provides a composition containing thymol in combination with a sufficient amount of sodium chloride and a sufficient amount of menthyl lactate for effectively masking the taste perception of thymol. This combination of sodium chloride and menthyl lactate in the composition containing thymol effectively masks the harsh, medicinal flavor or taste of thymol without the need for additional intense flavorants such as for example spearmint, peppermint, and the like.

In another embodiment the present invention provides an oral hygienic composition comprising effective amounts of thymol, sodium chloride and menthyl lactate and other essential oils in which the harsh medicinal taste of thymol is effectively masked. In particular, the composition which comprises thymol, sodium chloride, menthyl lactate in admixture with eucalyptol, menthol, benzoic acid, menthyl salicylate, ethanol, and, optionally, a surfactant or mixture of surfactants.

Therefore, another embodiment of the invention provides an oral hygiene composition comprising:

- (a) about 0.02% to about 0.1% (w/v) of thymol;
- (b) about 0.1% to about 1.0% (w/v) of sodium
   chloride;
- (c) about 0.002% to about 0.06% (w/v) of menthyl lactate;
  - (d) about 0.04% to about 0.12% (w/v) of eucalyptol;
  - (e) about 0.02% to about 0.07% (w/v) of menthol;

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(f) about 0.05% to about 1.1% (w/v) of benzoic
 acid;

- (g) about 0.02% to about 0.09% (w/v) of methyl
  salicylate;
- (h) about 5% to about 35% (w/v) of ethanol; and
- (i) optionally, about 0.05% to about 8% (w/v) by weight surfactant; the unpleasant taste of the thymol constituent being masked by the combined sodium chloride and menthyl lactate; and the weight percentage of the ingredients being related to the weight of the composition.

still another embodiment of this invention is
directed to a method for masking the taste of thymol in a
composition or a final product. Accordingly, the method
comprises adding an effective amount of sodium chloride
and an effective amount of menthyl lactate to the
product. Preferredly, the weight ratio of the sodium
chloride to thymol ranges from about 5:1 to about 10:1
and the weight ratio of the menthyl chloride ranges from
0.1:1 to about 0.6:1.

The most preferred ratio of the sodium chloride to the thymol is about 7.8 to about 1, and the most preferred ratio of the menthyl lactate to the thymol is about 0.3 to about 1.

## DETAILED DESCRIPTION OF THE INVENTION

As will be appreciated by those skilled in the art, the threshold of perception of various types of flavoring agents is different among consumers, depending on the individual as well as accustomed tastes. Consequently, the level of menthyl lactate utilized in the inventive composition may range from a minimal to no perceived menthyl lactate flavor optionally the present invention will provide a composition with a mild, pleasant, subtle menthyl lactate taste, particularly in combination with the taste of salt (NaCl).

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In the compositions of this invention, the preferred ratio of sodium chloride to the thymol is from about 7.8 to about 1. The preferred ratio of the menthyl lactate to the thymol is from about 0.3 to about 1.

The compositions of this invention may, in 5 addition to the thymol, include effective amounts of other essential oils such as those selected from the group consisting of eucalyptus, menthol, methyl salicylate, and the like, and mixtures thereof. Generally, the total amount of essential oils present in 10 a composition, exclusive of the thymol, can be from about 0.05 to about 0.35% (w/v), based on the volume of the composition, with about 0.12 to about 0.28% (w/v) being preferred. For example, the compositions, as stated above, can contain eucalyptol, menthol, and methyl 15 salicylate. Preferably the eucalyptol is present in amounts of about 0.07 to about 0.11% (w/v) being preferred and most preferably about 0.08 to about 0.10% (w/v); preferably menthol is present in amounts of about 0.03% to about 0.06% (w/v) and most preferably about 0.04 20 to about 0.05% (w/v); and preferably methyl salicylate is present in amounts of about 0.03 to about 0.08% (w/v) and most preferably about 0.04 to about 0.07% (w/v); based on the total volume of the composition. In addition to the essential oils, benzoic acid is preferably present in 25 amounts of about 0.1 to about 0.2% (w/v), based on the total volume composition and most preferably about 0.13 to about 0.18% (W/V).

Compositions or final products containing thymol in which the taste of thymol is masked by the presence of the sodium chloride and the menthyl lactate, include oral preparations such as a mouthwash, spray or rinse, candies, gums, toothpaste.

In such preparations the vehicle -- i.e. the

carrier for the ingredients of the mouthwash, such a the

essential oils, and the like -- is typically a water
alcohol mixture. Generally the ratio of water to alcohol

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is in the range of from about 1:1 to about 20:1, preferably about 3:1 to about 20:1 and most preferably about 3:1 to about 10:1 by weight. The total amount of water-alcohol mixture in a mouthwash preparation is typically in the range from about 50% to about 99.9% by weight of the composition. The pH value of such mouthwash preparations is generally from about 3.5 to about 8.0 and preferably from about 4 to about 7.5. A pH below 3.5 would be irritating to the oral cavity and soften tooth enamel. A pH greater than 8 would result in an unpleasant mouth feel.

Oral liquid preparations may also contain surface active agents -- i.e. surfactants -- in amounts up to about 5% and fluorine-providing compounds in amounts up to about 2% (w/v) of the preparation.

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Surface active agents (surfactants) are organic materials which aid in the complete dispersion of the preparation throughout the oral cavity. The organic surface active material may be anionic, non-ionic, ampholytic, or cationic. Suitable anionic surfactants are water-soluble salts of higher fatty acid monoglyceride monosulfates, such as the sodium salt of of the monosulfated monoglyceride of hydrogenated coconut oil fatty acids; higher alkyl sulfates, such as sodium lauryl sulfate; alkyl aryl sulfonates, such as sodium dodecyl benzene sulfonate; higher alkyl sulfonacetates; higher fatty acid esters of 1.2-dihydroxy propane sulfonates; and substantially saturated higher aliphatic acyl amides of lower aliphatic amino carboxylic acids such as those having 12 to 16 carbons at the fatty acid, alkyl or acyl radicals. Examples of the last mentioned amides are N-lauroyl sarcosine, and the sodium, potassium, and ethanolamide salts of N-lauroyl, Nmyristyl or N-palmitoyl sarcosine.

The non-ionic surfactants employed are poly(oxyethylene)-poly(oxylpropylene) block copolymers. Such copolymers are known commercially as poloxamers and

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are produced in a wide range of structures and molecular weights with varying contents of ethylene oxide and propylene oxide. The non-ionic poloxamers according to the invention are non-toxic and acceptable as direct food additives. They are stable and readily dispersible in aqueous systems and are compatible with a wide variety of formulating ingredients for oral preparations. These surfactants should have an HLB (Hydrophilic-Lipophilic Balance) of between about 10 and 30 and preferably between 10 and 25.

Thus, non-ionic surfactants useful in this invention include poloxamers:

	105	188	284
	108	215	288
15	123	217	334
	124	234	335
	183	235	338
	184	237	407
	185	238	

20 Generally these polymers should constitute from 0.2% to 2% by weight of total volume of liquid oral preparation (% w/v) and preferably from 0.5% to 1% w/v. A particularly preferred poloxamer is Poloxamer 407 having an HLB of about 22. Such a polymer is sold under the trademark Pluronic F-127 (BASF-WYAN-DOTTE).

Another class of non-ionic surfactants useful in this invention are ethoxylated hydrogenated castor oils. Such surfactants are prepared by hydrogenating castor oil and treating the so-formed product with from about 10 to 200 moles of ethylene glycol. They are designated as PEG (numeral) hydrogenated castor oil in accordance with the dictionary of the Cosmetics, Toiletries and Fragrance Association, 3rd Ed. wherein the numeral following PEG indicates the degree of ethoxylation, i.e. the number of moles of ethylene oxide added. Suitable PEG hydrogenated castor oils include PEG 16, 20, 25, 30, 40, 50, 60, 80, 100 and 200. The

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ethoxylated hydrogenated castor oils are used in the same concentrations as the above described poly(oxyethylene) - poly(oxypropylene) block copolymers.

Other non-ionic surface active agents which may be suitable include codensates of sorbitan esters of fatty acids with from 20 to 60 moles of ethylene oxide (e.g. "Tween" a trademark of ICI United states, Inc.), and amphoteric agents such as quaternized imidazole derivatives.

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Additional non-ionic surfactants which may be suitable are the condensation products of an alpha-olefin oxice containing 10 to 20 carbon atomes, a polyhydric alcohol containing 2 to 10 carbons and 2 to 6 hydroxyl groups and either ethylene oxide or a heteric mixture of ethylene oxide and propylene oxide. The resultant surfactants are polymers having a molecular weight in the range of 400 to about 1600 and containing 40% to 80% (w/v) of ethylene oxide, with an alpha-olefin oxide to polyhydric alcohol mole ratio in the range of about 1:1 to 1:3.

Cationic surface active agents which may be suitable are molecules that carry a positive charge such as cetylpyridinium chloride.

Fluorine providing compounds may be present in the oral preparations of this invention. These compounds may be slightly water soluble or may be fully water—soluble and are characterized by their ability to release fluoride ions or fluoride containing ions in water. Typical fluorine providing compounds are inorganic fluoride salts such as soluble alkali metal, alkaline earth metal, and heavy metal salts, for example, sodium fluoride, potassium floride, ammonium fluoride, cuprous fluoride, zinc fluoride, stannic fluoride, stannous fluoride, barium fluoride, sodium fluorosilicate, ammonium fluorosilicate, sodium fluorozirconate, sodium monofluorophosphate, aluminum mono- and difluorophosphate and fluorinated sodium calcium pyrophosphate.

Alkali metal, tin fluoride and monofluorophosphates such as sodium and stannous fluoride, sodium monofluorophosphate and mixtures thereof are preferred.

In an oral liquid preparation such as a mouthwash, the fluorine porviding compound is generally present in an amount sufficient to release up to about 0.15%, preferably about 0.001% to about 0.1% and most preferably from about 0.001% to about 0.05% fluoride weight/volume of the preparation.

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If desired, auxiliary sweetners may be utilized in the compositions of this invention. Those sweeteners which may be included are those well known in the art, including both natural and artificial sweeteners.

The sweetening agent (sweetener) used may be selected from a wide range of materials including water-soluble sweetening agents, water-soluble artificial sweeteners, water-soluble sweetening agents derived form naturally occurring water-soluble sweeteners, dipeptide based sweeteners, and protein based sweeteners, including mixtures thereof. Without being limited to particular sweeteners, representative illustrations encompass:

- A. Water-soluble sweetening agents such as monosaccharides, disaccharides and polysaccharides such as xylose, ribose, glucose (dextrose), mannose, galactose, fructose (levulose), sucrose (sugar), maltose, invert sugar (a mixture of fructose and glucoses derived from sucrose), partially hydrolyzed starch, corn syrup solids, dihydrochalcones, monellin, steviosides, aand glycyrrhizin;
- B. Water-soluble artificial sweeteners such as the soluble saccharin salts, i.e. sodium or calcium saccharin salts, cyclamate salts, the sodium, ammonium or calcium salt of 3,4-dihydro-6-methyl-1,2,3-oxathiazine-4-one-2,2-dioxide, the potassium salt of 3,4-dihydro-6-methyl-1,2,3-oxathiazine-4-one-2,2-dioxide (acesulfame-K), the free acid form saccharine, and the like;

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- aspartic acid derived sweeteners, such as L-aspartyl-L-phenylalanine methyl ester (aspartame) and materials described in U.S. Pat. No. 3,492,131,L-alpha-aspartyl-N-(2,2,4,4-tetramethyl-3-thietanyl)-D-alaninamide hydrate, methyl esters of L-aspartyl-L-phenylglycerine and L-aspartyl-2,5-dihydro-L-phenylalanine; L-aspartyl-L-(1-cyclohexyenh)-alanine; and the like:
- D. Water-soluble sweeteners derived from
  naturally occurring water-soluble sweeteners, such as a
  chlorinated derivative of ordinary sugar (sucrose),
  known, for example, under the product description of
  sucralose; and
- E. Protein based sweeteners such as thaumatoccous danielli (Thaumatin I and II).

In general, an effective amount of auxiliary sweetener is utilized to provide the level of sweetness desired for a particular composition and this amount will vary with the sweetener selected. This amount will normally be 0.01% to about 40% weight per volume 20 (hereinafter: w/v) of the composition when using an easily extractable sweetener. The water soluble sweeteners described in category A above, are usually used in amounts of about 5% to about 40% (w/v), and preferably in amounts of about 10% to about 20% (w/v) of 25 the final composition. Some of the sweeteners in category A (e.g., glycyrrhizin) may be used in amounts set forth for categories B-E below due to the sweeteners' known sweetening ability. In contrast, the sweeteners described in categories B-E are generally used in amounts 30 of about 0.005% to about 5.0% (w/v) of the final composition without about 0.03% to about 2.5% (w/v) being usual and about 0.03 to about 0.4% (w/v) being preferred. These amounts may be used to achieve a desired level of sweetness independent from the flavor level achieved from 35 any optional flavor oils used.

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The use of the sodium chloride and the menthyl lactate, as discussed above, results in the successful taste masking of the thymol taste. The compositions so masked have a pleasing taste, and, depending on the threshold level of perception of the consumer, may have a slight pleasing anise-like flavor perception. Therefore, additional flavorants or flavors are not necessary; however, if desirable, additional flavorings (flavors) may be added.

The flavorings (flavoring agents) that may be 10 used include those known to the skilled artisan, such as, natural and artificial flavors. These flavorings may be chosen from synthetic flavor oils and flavoring aromatics, and/or oils, oleo resins and extracts derived from plants, leaves, flowers, fruits and so forth, and 15 combinations thereof. Representative flavor oils include: spearmint oil, cinnamon oil, oil of wintergreen (methyl salicylate), peppermint oil, clove oil, bay oil, eucalyptus oil, thyme oil, cedar leaf oil, coriander oil, 20 pimento oil, sassafras oil, aniseed oil, oil of nutmeg, oil of sage, and oil of bitter almonds. Also useful are artificial, natural or synthetic fruit flavors such as vanilla, and citrus oil, including lemon, orange, lime and grapefruit and fruit essences including apple, grape, pear, peach, strawberry, raspberry, cherry, plum, 25 pineapple, apricot and so forth. These flavorings may be used individually or in admixture. Commonly used flavors include mints such as peppermint, menthol, artificial vanilla, cinnamon derivatives, and various fruit flavors, whether employed individually or in admixture. 30

Flavorings such as aldehydes and esters including cinnamyl acetate, cinnamaldehyde, citral, diethylacetal, dihydrocarvyl acetate, eugenol formate, pmethylanisole, and so forth may also be used. Generally any flavoring or food additive such as those described in Chemicals Used in Food Processing, pub 1274 by the National Academy of Sciences, pages 63-258 may be used.

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Further examples of aldehyde flavorings include, but are not limited to acetaldehyde (fruit); benzaldehyde (cherry almond); cinnamic aldehyde (cinnamon); citral, i.e., alpha citral (lemon, lime); neral, i.e. beta citral (lemon, lime); decanal (orange, lemon); ethyl vanillin (vanilla, cream); heliotropin i.e. piperonal (vanilla cream); vanillin (vanilla cream); alpha-amyl cinnamaldehyde (spicy fruity flavors); butyraldehyde (butter, cheese); valeraldehyde (butter, cheese); citronellal (modifies, many types); decanal 10 (citrus fruits); aldehyde C-8 (citrus fruits); aldehyde C-9 (citrus fruits); aldehyde C-12 (citrus fruits); 2ethyl butyraldehyde (berry fruits); hexenal, i.e. trans-2 (berry fruits); tolyl aldehyde (cherry, almond); veratraldehyde (vanilla); 2,6-dimethyl-5-heptenal, i.e. 15 melonal (melon); 2-6-dimethyloctanal (green fruit); and 2-dodecenal (citrus, mandarin); cherry; grape; mixtures thereof; and the like.

The amount of flavoring employed is normally a matter of preference subject to such factors as flavor profile type, individual flavor, and strength desired. thus, the amount may be varied in order to obtain the result desired in the final product. Such variations are within the capabilities of those skilled in the art without the need for undue experimentation. In general, amounts of about 0.05% to about 2.0% by weight of the composition are useable with amounts of about 0.05% to about 1.5% being preferred.

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The compositions of this invention may also contain coloring agents or colorants.

The coloring agents are used in amounts effective to produce the desired color. The coloring agents (colorants) useful in the present invention, include the pigments such as titanium dioxide, which may be incorporated in amounts of up to about 2% by weight of the composition, and preferably less than about 1% by weight. Colorants may also include natural food colors

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and dyes suitable for food, drug and cosmetic applications. These colorants are known as F.D. & C. dyes and lakes. The materials acceptable for the foregoing spectrum of use are preferably water-soluble, and include indigoid dye, known as F.D. & C. Blue No. 2, 5 which is the disodium salt of 5,5-indigotindisulfonic Similarly, the dye known as Green No. 1 comprises a triphenylmethane dye and is the monosodium salt of 4-[4-N-ethyl-p-sulfobenzylamino) diphenylmethylene]-[1-Nethyl-N-p-sulfoniumbenzyl(-delta2.5-cyclohexadienimine). 10 Additional examples include the yellow dye, known as D&C Yellow No. 10, and the dye known as F.D. & C. Green No. 3 which comprises a triphenylmethane dye. A full recitation of all F.C. & C. and D. & C. dyes and their corresponding chemical structures may be found in the 15 Kirk-Othmer Encyclopedia of Chemical Technology, Volume 5, Pages 857-884, which text is accordingly incorporated herein by reference.

The oral compositions of this invention may also be substantially solid or pasty in character such as 20 a dental cream, toothpaste, or a toothpowder. Solid or pasty oral preparations contain polishing materials. Typical polishing materials are abrasive particulate materials having particle sizes of up to about 20 25 microns. Nonlimiting illustrative examples include: water-insoluble sodium metaphosphate, potassium metaphosphate, tricalcium phosphate, dihydrated calcium phosphate, calcium pyrophosphate, magnesium orthophosphate, trimagnesium phosphate, calcium 30 carbonate, alumina, aluminum silicate, zirconium silicates, silica, bentonite, and mixtures thereof. Polishing materials are generally present in an amount from about 20% to about 82% weight per volume of the oral preparation. Preferably, they are present in amounts 35 from about 20% to about 75% in toothpaste, and from about 70% to about 82% in toothpowder. For toothpaste and

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dental creams the water content is about 25% to 50% (w/v).

In clear gels, a polishing agent of colloidal silica and alkali metal aluminosilicate complexes are preferred since they have refractive indices close to the refractive indices of gelling agent liquid systems commonly used in dentifrices.

In the oral preparation that are toothpastes, dental creams, or gels the liquid vehicle may comprise water, typically in an amount of about 10-90% weight per 10 volume of the composition. Polyethylene glycol, propylene glycol, glycerin or mixtures thereof may also be present as humectants or binders in amounts of about 20-25% by weight. Particularly advantageous liquid 15 ingredients comprise mixtures of water with polyethylene glycol or glycerin and propylene glycol. A gelling agent (thickening agent) including natural or synthetic gums such as sodium carboxymethylcellulose, hydroxyethylcellulose, methyl cellulose and the like may 20 be used, in the range of about 0.5-5% by weight. toothpaste, dental cream or gel, the liquids and solids are proportioned to form a creamy or gelled mass which is extrudable from a pressurized container or from a collapsible tube.

The toothpaste or gel may also contin a surface active agent which may be an anionic, nonionic or zwitterionic detergent (surfactant) in amounts of about 0.05-5% (w/v). The anionic and nonionic surfactants that are suitable have already been discussed above.

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Zwitterionic surface active agents include the betaines and sulfobetaines. Typical alkyl dimethyl betaines include decyl betaine or 2-(N-decyl-N,N-dimethylammonio) acetate, coco betaine, myristyl betaine, palmityl betaine, lauryl betaine, cetyl betaine, stearyl betaine, etc. The amidobetaines similarly include cocoamidoethyl betaine, cocoamidopropyl betaine, lauramidopropyl betaine and the like. These

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sulfobetaines are similar in structure to the betaines, but have a sulfonate group in place of the carboxylate group, and include alkylsulfobetaines, alkylamidosulfobetaines and alkylaminosulfobetaines.

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In general, the compositions of this invention are prepared utilizing techniques well known to those skilled in the art. Thus, the liquid compositions may be prepared by mixing the alcohol soluble ingredients with ethanol, adding a quantity of water to the mixture thus obtained, and then blending or mixing in the water soluble ingredients. For example, in preparing one liter of a typical liquid oral composition, thymol, eucalyptol, menthol, methyl salicylate, surfactant, and benzoic acid are dissolved in and mixed with ethanol. To this resulting mixture a sufficient quantity of water is added, and then the auxiliary sweetener, water soluble colorants, buffers, and the like are blended in. Then additional water is added to make up one liter.

Those skilled in the art will appreciate that the total amount of all ingredients (components) used in the compositions of this invention equals 100% weight per volume of the total composition. Also, unless state otherwise, all percents herein are weight percent per volume of the total composition.

The following examples are illustrative only and should not be construed as limiting the invention in any way. Those skilled in the art will appreciate that variations are possible which are within the spirit and scope of the appended claims.

In the examples that follow, the compositions were prepared by blending the thymol, eucalyptol, menthol, methylsalicylate, ethanol and surfactant mixed with the ethanol. To the resulting mixture about 300 ml. of water was mixed therewith and then the examining water soluble ingredients were added - e.g. the sodium saccharin, buffers (citric acid and sodium citrate), the colorants and the like - and blended in. To this

resulting mixture, enough water was added to make on liter of solution. Prior to taste evaluation, all compositions were aged a minimum of 5 days at room temperature.

TABLE I

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Ingredient	Unit	Example A	Example 1	Example B	Example 2
Thymol	g	0.639	0.639	0.639	0.639
Benzoic Acid	g	1.5	1.5	5.0	5.0
Sodium Chloride	g	0	5.0	0	5.0
Menthyl Lactate	g	· 0	0.2	0	0.2
Alcohol	mL	195	195	195	195
Menthol	g	0.425	0.425	0.425	0.425
Eucalyptol	g	0.922	0.922	0.922	0.922
Methyl Salicylate	g	0.600	0.600	0.600	0.600
Pluronic F-127	g	1.0	1.0	1.0	1.0
Sodium Lauryl Sulfate	g	1.5	1.5	1.5	1.5
Sodium Saccharin	g	1.5	1.5	1.5	1.5
Propylene Glycol	g	20	20	20	20
Water qs to	L	1	1	1	1

Table 1 shows the compositions of a comparative expedient for mouth wash where Example A, Example 1, Example B, and Example 2 are listed. The 25 examples were evaluated in a blind test by rating the taste of the composition of Example 1 or Example 2 which are in accordance with the present invention, in comparison with the taste of the control Example A and Example B, respectively. Example 2 differs from Example

1 by a greater benzoic acid content, i.e., 0.5% vs.
0.15% weight/volume. The comparative taste quality of
Example 1 v. Example A is rated as to having "more
thymol taste" or "less thymol taste". As to taste for
5 Example 2 compared to control Example B, value number
one (1) means "more harsh" and number nine (9) means
"less harsh". Value five (5) is representative of
having no difference in taste between control and
inventive example. Accordingly, the flavor perceptions
10 were as follows:

#### Part 1:

Example 1 - less harsh, mild, less thymol taste
with some salty taste; not as bitter or
dehydrating;

Example A - a comparative non-inventive control composition similar to Example 1 except that the formulation of Example A contained no sodium chloride and no menthyl lactate. The formulation was found to have an intolerably harsh thymol taste.

#### Part 2:

Example 2 - milder overall, not as harsh and
astringent but pleasant combination with the tastes
of sweetness and saltiness being tolerable.

Example B - a comparative, non-inventive control composition similar to Example 2 but lacking sodium chloride and menthyl lactate. The formulation was found to be very harsh, almost not tolerable, in fact, irritating.

#### 30 METHOD OF TASTE TESTING

The test participants were asked to determine blindlythe taste of thymol in the examples (i.e. Ex. 1 and 2) in comparison with the corresponding negative control examples (i.e. Ex. A and B). The perceived 35 thymol taste was rated on a scale of 1-10, where 1 was equivalent to more and 10 to less thymol taste while 5 signified no difference in thymol taste. The results

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are shown in Table II, indicating clear improvements of masking thymol taste in the two embodiments represented by Example 1 and Example 2.

The numerical values of the Examples 1 and 2 according 5 to the present invention were assigned by six individual panel numbers as listed in Table II.

TABLE II

_	Test Person	Ouestion Part 1	Part 2
	. 1	8	7
10	2	9	8
	3	7	7
	4	7	5
	5	3	5
	6	7	8
15			
	i	Ave. 6.8	7.2

The invention thus being described, it will be obvious that the same may be varied in many ways. Such 20 variations are not to be regarded as a departure from the spirit and scope of the invention. All such modifications are intended to be included with the scope of the claims.

#### WHAT IS CLAIMED IS:

- An aqueous composition containing thymol formulated for masking the harsh, medicinal taste of thymol comprising effective amounts of sodium chloride and
   menthyl lactate.
  - 2. The aqueous composition as in claim 1, further comprising a mixture of ingredients containing, in addition to thymol, essential oils, benzoic acid, ethanol, and a surfactant or a blend of surfactants.
- 10 3. The aqueous composition as in claim 2 wherein the essential oils comprise eucalyptol, menthol and methyl salicylate.
  - 4. The aqueous composition as in claim 2 wherein the surfactant or blend of surfactants selected from the
- 15 group consisting of anionic, non-ionic, and cationic surfactants.
  - 5. The aqueous composition as in claim 4 wherein the surfactant is a non-ionic surfactant.
- 6. The aqueous composition as in claim 1 wherein the 20 amount of sodium chloride has a weight ratio ranging from about 5:1 to about 10:1 relative to the thymol and wherein the amount of menthyl lactate has a weight ratio relative to the thymol ranging from about 0.1:1 to about 0.6:1.
- 25 7. The aqueous composition as in claim 6 wherein the weight ratio of sodium chloride to thymol is about 7.8 to 1 and the weight ratio of menthyl lactate to thymol is about 0.3 to 1.
  - 8. An aqueous final product containing thymol
- 30 formulated for masking the harsh, medicinal taste of thymol comprising effective amounts of sodium chloride and menthyl lactate in a mixture of thymol, menthol, eucalyptol, methyl salicylate, ethyl alcohol, propylene glycol, benzoic acid, sodium saccharin, poloxomer having 35 an HLB of about 22, and water.
  - 9. The aqueous final product of claim 8, wherein the effective amounts of sodium chloride and menthyl lactate

- are each at a weight ratio to the thymol ranging from about 5:1 to about 10:1 and from about 0.1:1 to about 0.6:1, respectively.
- 10. The aqueous final product of claim 9, wherein the 5 weight ratio of sodium chloride to thymol is about 7.8:1 and the weight ratio of menthyl lactate to thymol is about 0.3:1.
  - 11. A method for masking the medicinal, harsh taste of thymol in an aqueous composition, comprised of adding
- 10 effective amounts of sodium chloride and menthyl lactate, in combination, to a mixture comprising in addition to thymol, essential oils, benzoic acid, ethyl alcohol, and surfactant or a blend of surfactants, and water.
- 15 12. The method as claimed in claim 11, wherein the sodium chloride is added at a weight ratio to the thymol ranging from about 5:1 to about 10:1 and the menthyl lactate is added at a weight ratio to the thymol ranging from about 0.1:1 to about 0.6:1.
- 20 13. The method as claimed in claim 11 wherein the sodium chloride has weight ratio of thymol of about 7.8 to 1 and the menthyl lactate has a weight ratio to thymol of about 0.3 to 1.
- 14. The method as claimed in claim 11, wherein the
- 25 essential oils are comprised of about 0.02% to about 0.1% (w/v) thymol, about 0.04% to about 0.12% (w/v) eucalyptol, about 0.02% to about 0.07% (w/v) menthol and about 0.02% to about 0.09% (w/v) methyl salicylate; and wherein the benzoic acid ranges from about 0.05% to
- 30 about 0.25% (w/v); wherein the ethyl alcohol is from about 5% to about 35% (w/v); the percentages being based on the total volume of the aqueous composition.
  - 15. A method for preparing a final product according to claim 11.
- 35 16. A method for masking the medicinal, harsh taste of thymol in an aqueous final product, comprised of adding effective amounts of sodium chloride and menthyl lactate

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to a mixture comprising thymol, menthol, eucalyptol, methyl salicylate, ethyl alcohol, propylene glycol, benzoic acid, sodium lauryl sulfate, sodium saccharin, poloxomer having an HLB of about 22 and water.

of 17. The method as claimed in claim 14, wherein the effective amounts of sodium chloride and menthyl lactate are each added at a weight ratio to the thymol ranging from about 5:1 to about 10:1 and from about 0.1:1 to about 0.6:1, respectively.

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## INTERNATIONAL SEARCH REPORT

Int. .ional Application No PCT/US 93/09441

A. CLASS IPC 5	SIFICATION OF SUBJECT MATTER A61K31/05 A61K9/00 A61K47/	no A61K47/14	
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	to International Patent Classification (IPC) or to both national class	ification and IPC	·
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	MENTS CONSIDERED TO BE RELEVANT		M Nia
Category *	Citation of document, with indication, where appropriate, of the	relevant passages	Relevant to claim No.
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A	US,A,4 945 087 (A.K.TALWAR) 31 J	nih taan	1-1/
	see the whole document		
i			
A	EP,A,O 371 584 (WARNER-LAMBERT)	6 June	1-17
	1990 see the whole document		
	See the whole document		
A	US,A,4 983 394 (M.M.HUSSEIN) 8 J	anuary	1-17
	1991 see the whole document	·	1
	see the whole document		·
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Furt	her documents are listed in the continuation of box C.	X Patent family members are listed in	annex.
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## INTERNATIONAL SEARCH REPORT

Information on patent family members

In. ional Application No PCT/US 93/09441

Patent document cited in search report	. Publication date	Patent family member(s)		Publication date
US-A-4945087	31-07-90	AU-A- EP-A,B JP-A- JP-B-	3160289 0338978 1287016 4063045	05-10-89 25-10-89 17-11-89 08-10-92
EP-A-0371584	06-06-90	US-A- AU-A- JP-A-	5013716 4387689 2177870	07-05-91 03-05-90 10-07-90
US-A-4983394	08-01-91	EP-A- JP-A-	0455599 4228033	06-11-91 18-08-92